

WE CLAIM

1. A composition for generating a metal ion labeled imaging agent, the composition comprising:

- a metal support surface; and

- 5 • a conjugate including a metal ion binding moiety and a biological targeting moiety, the metal ion binding moiety including a sulfur atom or a phosphorous atom for binding to the metal support surface,

10 wherein the metal ion binding moiety is capable of coordinating with a metal ion when the metal ion binding moiety is bound to the support thereby releasing the labeled conjugate from the support surface.

2. The compound of claim 1, wherein the metal ion binding moiety includes a sulfur atom attached to a sulfur protecting group, the metal support surface being capable of binding to the protected sulfur atom thereby releasing the sulfur protecting group from the sulfur atom and forming a thiol bond with the metal ion binding moiety.

- 15 3. The compound of claim 2 wherein the metal support surface is gold.

4. The compound of claim 1, wherein the metal support surface comprises a metal capable of releasably binding sulfur or phosphorous for forming a metal ion labeled agent.

- 20 5. The compound of claim 1, wherein the support surface comprises a metal selected from the group consisting of gold, silver and copper

6. The compound of claim 1, wherein the conjugate comprises a ligand and a targeting molecule wherein the ligand incorporates:

25 (a) a surface binding group selected from the group consisting of a cysteine amino acid residue, a cysteine amino acid residue derivative, a thiol or thioether group attached to an organic molecule, an amino acid residue derivative

including phosphorous and a phosphorous containing organic molecule, wherein the amino acid residue, amino acid residue derivative or organic molecule is capable of releasably binding to the support surface; and

5 (b) at least one accessory group capable of coordinating with the complex-forming metal ion;

wherein the conjugate is capable of coordinating with a complex-forming metal ion so that the conjugate is released from the support surface.

10 7. A compound useful for generating a complex-forming metal ion labeled agent, the compound comprising: a metal support surface capable of releasably coordinating to sulfur or phosphorus, and a conjugate releasably bound to the support surface, the conjugate comprising a ligand and a targeting molecule wherein the ligand incorporates

15 (a) a surface binding group selected from the group consisting of a cysteine amino acid residue, a cysteine amino acid residue derivative, a thiol or thioether group attached to an organic molecule, an amino acid residue derivative including phosphorous and a phosphorous containing organic molecule, wherein the amino acid residue, amino acid residue derivative or organic molecule is capable of releasably binding to the support surface; and

(b) at least one accessory group capable of coordinating with the complex-forming metal ion;

20 wherein the conjugate is capable of coordinating with a complex-forming metal ion so that the conjugate is released from the support surface.

8. The compound claim 7, wherein the ligand comprises a peptide, a peptide mimetic, a polypeptide, a polypeptide mimetic or a small organic molecule.

25 9. The compound of any of claims 7 or 8 wherein the targeting molecule comprises a molecule having agonist or antagonist activity selected from the group consisting of a polypeptide, a peptide, a nucleic acid molecule, an oligonucleotide, a saccharide, an

oligosaccharide, a steroid, a cyclic peptide, a peptide or polypeptide mimetic, an enzyme substrate, an inhibitor and a small organic molecule.

10. The compound of any of claims 7 to 9, wherein the targeting molecule comprises a peptide, a polypeptide, a peptide or polypeptide mimetic or a small organic molecule.
- 5 11. The compound of any of claims 1 to 10, wherein the conjugate comprises a peptide, a polypeptide, a peptide or polypeptide mimetic or a small organic molecule.
12. The compound of any of claims 7 to 11, wherein the ligand comprises a peptide selected from the group consisting of a tetradentate N_xS_{4-x} ligand, a tetradentate N_xS_{4-x} ligand derivative, a polyamino polysulfide and a polyamino polysulfide derivative.
- 10 13. The compound of any of claims 1 to 12, wherein the targeting molecule comprises a molecule selected from the group consisting of a bombesin 7-14 fragment, QWAVGHLM, TKPPR, RGDS and a small organic molecule that targets a receptor or a transporter.
- 15 14. The compound of any of claims 1 to 13, wherein the conjugate comprises a peptide sequence selected from the group consisting of a bombesin 7-14 fragment, QWAVGHLM, TKPPR, RGDS and small organic molecule that targets a receptor or a transporter.
- 20 15. The compound of claim 13 or 14, wherein the receptor or transporter is selected from the group consisting of a dopamine receptor or transporter, a serotonin receptor or transporter, a sigma receptor, a GABA receptor, a nicotinic receptor, a cholinergic receptor, a norepinephrine receptor or transporter, a glucose transporter and an opioid receptor.
- 25 16. The compound of any of claims 7 to 15, wherein the ligand incorporates 3 accessory groups selected from the group consisting of (a) a nitrogen atom, an oxygen atom or a sulfur atom incorporated in an amino acid residue, (b) a nitrogen atom, an oxygen atom, a selenium atom, a phosphorous atom or a sulfur atom incorporated in an amino acid residue derivative, or (c) a nitrogen atom, an oxygen atom, a selenium atom, a phosphorous atom or a sulfur atom incorporated in an organic molecule or (d) a

combination of one or more of (a) to (c), wherein the residues, derivatives and/or molecules have metal coordinating activity.

17. The compound of claim 16, wherein the metal support surface comprises a metal selected from the group consisting of gold, silver and copper.
- 5 18. The compound of any of claims 1 to 17, wherein the complex-forming metal is selected from the group of metals and radioisotopic metals consisting of Tc, Re, Mn, Fe, Co, Ni, Zn, Cd, Mo, W, Cu, Ag, Au, Ti, Hg, Cr and Rh.
19. The compound of any of claims 1 to 17, wherein the complex-forming metal is selected from the group of metals and radioisotopic metals consisting of Tc, Cu and Re.
- 10 20. A method for generating a complex-forming metal ion labeled diagnostic agent or radiotherapeutic agent, comprising the steps of: (a) providing a compound according to any of claims 1 to 19; (b) contacting the compound with the complex-forming metal ion to form a coordinate bond between the complex-forming metal ion and the agent so that the complex-forming metal labeled agent is released from the support
15 surface.
21. The method of claim 20, further comprising collecting the complex-forming metal labeled agent so released.
22. A method for generating a complex-forming metal ion labeled diagnostic agent or radiotherapeutic agent, comprising the step of transchelating a conjugate from a metal
20 support surface to a complex-forming metal ion so that the conjugate is released from the metal support surface.
23. A method for preparing a complex-forming metal ion labeled peptide comprising (a) bonding a peptide, polypeptide, peptide mimetic or polypeptide mimetic that includes (i) a cysteine amino acid residue, a cysteine amino acid residue derivative or a
25 phosphorous amino acid residue derivative and (ii) at least one accessory group capable of coordinating with the complex-forming metal ion, to a metal support surface by the sulfur atom or phosphorous atom of the residue or derivative and (b)

labeling the peptide, polypeptide or mimetic with a complex-forming metal so that the metal complexed peptide, polypeptide or mimetic is released from the support surface.

24. The method of claim 34, wherein peptide, polypeptide, peptide mimetic or polypeptide mimetic is between about 3 and 50 amino acid residues or amino acid residue derivatives.
25. A method for preparing a complex-forming metal ion labeled agent comprising the steps of (a) bonding an organic molecule that includes (i) a sulfur atom or a phosphorous atom and (ii) at least one accessory group capable of coordinating with the complex-forming metal ion, to a support surface by the sulfur atom or the phosphorous atom and (b) labeling the agent with a complex-forming metal so that the metal complex conjugate is released from the support surface.
26. The method of claim 25, wherein the peptide, polypeptide, peptide mimetic or polypeptide mimetic is between about 3 and 50 amino acid residues or amino acid residue derivatives.
27. The method of any of claims 22 to 26, wherein the support surface comprises a metal selected from the group consisting of gold, silver, copper and a metal capable of releasably binding sulfur or phosphorous for forming a metal complex; and the complex-forming metal is selected from the group of metals and radioisotopic metals consisting of Tc, Re, Mn, Fe, Co, Ni, Zn, Cd, Mo, W, Cu, Ag, Au, Ti, Hg, Cr and Rh.
28. A method for preparing a complex-forming metal ion labeled agent comprising the steps of (a) providing a conjugate including a metal ion binding moiety and a biological targeting moiety, the metal ion binding moiety including a sulfur atom for binding to the metal support surface, the sulfur atom being protected by a sulfur protecting group, (b) contacting the protected sulfur atom with the metal support surface so that the sulfur atom forms a thiol bond with the metal surface thereby releasing the sulfur protecting group and (c) contacting the metal ion binding moiety with the complex-forming metal ion to form a coordinate bond between the complex-forming metal ion and the metal ion binding moiety so that the complex-forming metal labeled agent is released from the support surface.

29. A method according to claim 28 wherein the metal support surface is gold.
30. A complex-forming metal ion labeled agent prepared according to the method of any of claims 20 to 29.
- 5 31. A composition for radiotherapy or imaging, comprising the agent of claim 30 and a carrier.
32. The composition of claim 31, further comprising an agent selected from the group consisting of a reducing agent, a bulking agent and a pH stabilising agent.
33. A pharmaceutical composition for radiotherapy or imaging, comprising the agent of claim 30 and a pharmaceutically suitable carrier.
- 10 34. A kit for preparing a complex-forming metal ion labeled agent, the kit comprising a metal support surface, a conjugate and a predetermined quantity of a complex-forming metal ion, the conjugate being capable of being releasably bound to the support surface and capable of coordinating with the complex-forming metal ion so that the conjugate is released from the metal support surface.
- 15 35. The kit of claim 34 wherein the conjugate includes a sulfur atom attached to a sulfur protecting group, the metal support surface being capable of binding to the protected sulfur atom thereby releasing the sulfur protecting group from the sulfur atom and forming a thiol bond with the conjugate.
- 20 36. The kit of claim 35, wherein the conjugate comprises a ligand and a targeting molecule wherein the ligand incorporates
- 25 (a) a surface binding group selected from the group consisting of a cysteine amino acid residue, a cysteine amino acid residue derivative, an organic thiol or thioether containing molecule, an amino acid residue derivative including phosphorous and a phosphorous containing aliphatic molecule, wherein the amino acid residue, amino acid residue derivative or aliphatic molecule is capable of releasably binding to the support surface; and

(b) at least one accessory group.

wherein the conjugate is capable of coordinating with a complex-forming metal so that the conjugate is released from the support surface.

- 5 37. The kit of claim 34 or 35, wherein the support surface comprises a metal selected from the group consisting of gold, silver, copper and a metal capable of releasably binding sulfur or phosphorous for forming a metal complex; and the complex-forming metal is selected from the group of metals and radioisotopic metals consisting of Tc, Re, Mn, Fe, Co, Ni, Zn, Cd, Mo, W, Cu, Ag, Au, Ti, Hg, Cr and Rh.
- 10 38. The kit of claim 34 or 35 further comprising an agent selected from the group consisting of a reducing agent, a bulking agent and a pH stabilising agent.
39. A method of detecting the presence or assessing the severity of a disease, disorder or abnormal physical state in a mammal comprising: (a) administering an effective amount of the agent or composition of any claims 30 to 32; and (b) detecting the presence or assessing the severity of the disease, disorder or abnormal physical state.
- 15 40. A method of radiotherapy of a disease, disorder or abnormal physical state in a mammal comprising administering an effective amount of the agent or composition of any claims 30 to 32.
41. The method of claim 39 or 40, wherein the complex-forming metal labeled imaging agent is administered by an intravenous route.
- 20 42. The method of any claims 39 to 41, wherein the amount of complex-forming metal labeled agent administered to the mammal is about 0.01 mcg/kg/minute to 1,000 mcg/kg/minute.
43. The method of claim 42, wherein the amount of complex-forming metal labeled agent administered to the mammal is about 0.01 to 50 mcg/kg/minutes.
- 25 44. The method of any of claims 39 to 43, wherein the mammal is a human.

45. The method of any of claims 39 to 44, wherein the disease, disorder or abnormal physical state is selected from the group consisting of oncological, neurological, inflammatory, infection, and degenerative diseases, disorders and abnormal physical states.
- 5 46. The method of claim 45, wherein the presence or severity of the disease, disorder or abnormal physical state is detected or assessed with a technique selected from the group consisting of positron emission tomography, nuclear magnetic resonance imaging, scintigraphy, single photon emission computed tomography, perfusion contrast echocardiography, ultrafast X-ray computed tomography, and digital subtraction angiography.
- 10 47. The method of claim 46, wherein the agent comprises a ^{99m}Tc metal and the agent binds to a receptor and the technique is single photon emission computed tomography.
- 15 48. A composition comprising a technetium metal labeled agent, wherein the composition includes a specific activity greater than 10,000 Ci/mmol with 99m-technetium and greater than 3,000 Ci/mmol with 188-rhenium
49. The composition of claim 48, wherein the agent is a peptide or polypeptide or a mimetic thereof.
50. The composition of claim 49, wherein the peptide comprises dimethylglycylserinylcysteinylglycine.
- 20 51. A method for the preparation of a support surface for manufacturing a complex-forming metal labeled agent comprising electro or electroless metal plating or vapor deposition of a suitable thickness, of the metal onto an inorganic or polymeric substrate in the form of particles, sponges or sieves, fibers or surfaces with suitable surface area between about 1 and 10,000cm².
- 25 52. The method of claim 51, wherein the thickness of the metal on the metal support surface is greater than about 10nm.

53. A pharmaceutical composition for radiotherapy or imaging, comprising a carrier and a complex-forming metal ion labeled agent, wherein the agent is prepared without HPLC.